

What Is Claim Is

1. A synthesis method of alanylglutamine, comprising the steps of:
 - 1) Formation of active ester by the reaction of 10 mmol N-terminal protected alanine, 10~30 mmol of triphenylphosphine and 10~30 mmol of hexachloroethane, in organic solvent for 20 min~3 hours, and reaction temperature is -5~30⁰C;
 - 2) In a liquid mixture made by mixing organic solvent and aqueous solution of inorganic base, the active ester obtained from step 1) reacts with 10~30 mmol of glutamine to form the N-terminal protected alanylglutamine, wherein the volume ratio of organic solvent and aqueous solution of inorganic base is 0~4, reaction temperature is -5~30⁰C, and pH is controlled at 8.5~13;
 - 3) Acidify the reaction mixture of step 2) with inorganic acid to pH≤3.0; and
 - 4) The alanylglutamine is obtained by removing the N-terminal protecting group with deprotecting reagent.
2. The synthesis method of alanylglutamine according to claim 1, characterized in that
 - 1) Formation of active ester by the reaction of 10 mmol of N-terminal protected alanine, 15~20 mmol of triphenylphosphine and 15~20 mmol of hexachloroethane in organic solvent for 1.5~2 hours, and reaction temperature is 0~10⁰C;
 - 2) In a liquid mixture made by mixing organic solvent and aqueous solution of inorganic base, the active ester obtained from step 1) reacts with 15~20 mmol of glutamine to form N-terminal protected alanylglutamine, wherein the volume ratio of organic solvent and aqueous solution of inorganic base is 0.5~2, reaction temperature is 5~10⁰C, and pH is controlled at 9.5~10.5;
 - 3) Alanylglutamine is obtained by acidifying the reaction mixture of step 2) to pH=2.0~3.0.
3. The synthesis method of alanylglutamine according to claim 1, characterized in that N-terminal protected alanine is N-(O,O-dimethyl) phosphoalanine (DMP-L-Ala), N-(O,O-diethyl) phosphoalanine (DEP-L-Ala), N-(O,O-diisopropyl) phosphoalanine

(DIPP-L-Ala), N-(O,O-di-n-butyl) phosphoalanine (DBP-Ala), carbobenzyloxyalanine (Z-L-Ala), (para-carbomethoxy) carbobenzyloxyalanine (MZ-L-Ala), tert-butylcarbonylalanine (Boc-L-Ala), or 2-(dibiphenyl) isopropylcarbonylalanine (Bpoc-L-Ala).

4. The synthesis method of alanylglutamine according to claim 1 or claim 2, characterized in that the organic solvent used in step 1) is selected from the group consisting of dichloromethane, toluene, tetrahydrofuran, acetonitrile or 1,2-dichloroethane.
5. The synthesis method of alanylglutamine according to claim 1 or claim 2, characterized in that the organic solvent used in step 2) is selected from the group consisting of ethanol ethyl acetate, petroleum ether, cyclohexane, toluene and dichloromethane.
6. The synthesis method of alanylglutamine according to claim 1 or claim 2, characterized in that the inorganic base used in step 2) is selected from the group consisting of sodium hydroxide, potassium hydroxide, sodium bicarbonate, potassium bicarbonate, sodium carbonate and potassium carbonate.
7. The synthesis method of alanylglutamine according to claim 1 or claim 2, characterized in that the inorganic acid used in step 3) is selected from the group consisting of hydrochloric acid, sulfuric acid, nitric acid and phosphoric acid.
8. The synthesis method of alanylglutamine according to claim 1 or claim 2, characterized in that the deprotective reagent is selected from the group consisting of trifluoroacetic acid, hydrogen chloride/glacial acetic acid, hydrogen bromide/glacial acetic acid, methyl sulfonic acid, hydrogenation reduction, hydrogen chloride/1,4-dioxane, hydrogen bromide/1,4-dioxane.

9. The synthesis method of alanylglutamine according to claim 1 or claim 2, characterized in that step 2) is accomplished as follows: the active ester obtained from step 1) reacts with glutamine in a stirring liquid mixture containing organic solvent and aqueous solution of inorganic base, and stirring and the condition of pH=9.5-10.5 must be maintained in the course of reaction.